DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Center for Devices and
Radiological Health
2098 Gaither Road
Rockville, MD 20850

NOV 9 2004

**WARNING LETTER**

**VIA FEDERAL EXPRESS**

Ilya Bragilevsky
Regulatory Affairs Officer
Germiphene Corporation
1379 Colborne Street East
Brantford, Ontario, Canada N3T5V7

Dear Mr. Bragilevsky:

During an inspection of your establishment located in Brantford, Ontario, Canada on June 14-16, 2004, our investigator determined that your firm manufactures dental device cleaners and ozonating water systems for dental use. Dental device cleaners and ozonation water systems are devices as defined by Section 201(h) of the Federal Food, Drug, and Cosmetic Act (the Act) (21 U.S.C. § 321(h)).

This inspection revealed that these devices appear to be adulterated within the meaning of section 501(h) of the Act (21 U.S.C. § 351(h)), in that the methods used in, or the facilities or controls used for, their manufacture, packing, storage, or installation are not in conformity with the Current Good Manufacturing Practice (CGMP) requirements of the Quality System (QS) regulation found at Title 21, Code of Federal Regulations (CFR), Part 820. Significant violations include, but are not limited to, the following:

1. Failure to adequately ensure that when the results of a process cannot be fully verified by subsequent inspection and test that the process shall be validated with a high degree of assurance and approved according to established procedure, as required by 21 CFR 820.75(a). For example, your firm's process validation for Gzyme, a dental device cleaning agent, is inadequate in that a) mixing time specifications for the addition and dissolving of enzymatic agents and other reagents in solution have not been established, and b) testing for activity or presence of enzymatic agents was not conducted.

2. Failure to establish and maintain procedures for receiving, reviewing, and evaluating complaints by a formally designated unit, as required by 21 CFR 820.198(a). For example, your firm had no written procedures for recording and handling of complaints for the Odyssey I device (ozonating water system).

3. Failure to designate an individual(s) to review for adequacy and approve prior to issuance all documents established to meet requirements of this part. All documents should include the date and signature as required by 21 CFR 820.40(a). For example, your firm had several quality documents and procedures in the Quality Manual which lack effective dates. These procedures include Internal Audits, non-conformance processes, and Corrective and Preventative Actions.

4. Failure to monitor and control process parameters, components, and device characteristics during production as required by 21 CFR 820.70(a)(2). For example, after a review of eleven Device History Records (DHR), it was revealed that in four instances the Gzyme device cleaner operators did not follow the listed one hour mixing time for dissolving the Blue FD&C1 and lemon fragrance mask. The listed mixing times recorded in the DHR were inconsistent, in which, some operators mixed for less than one hour and others mixed for more than one hour.

5. Failure to establish procedures for quality audits and conduct such audits to assure that the quality system is in compliance with the established quality system requirements, as required by 21 CFR 820.22. For example, your firm's internal audits were not reviewed and the sign off sheets indicating the audits were performed lacked the date and signature of the auditor.

We also note that you failed to develop, maintain, and implement written MDR procedures as required by 21 CFR 803.17. Specifically, your firm failed to have specific procedures for reporting adverse events to FDA, including the evaluation of adverse events received, the directions for reporting events within required time frames, and the method by which the events are reported.

This letter is not intended to be an all-inclusive list of violations at your facility. It is your responsibility to ensure compliance with applicable laws and regulations administered by FDA. The specific violations noted in this letter and in the Inspectional Observations, Form FDA 483 (FDA 483), issued at the closeout of the inspection may be symptomatic of serious problems in your firm's manufacturing and quality assurance systems. You should investigate and determine the causes of the violations, and take prompt actions to correct the violations and to bring your products into compliance.

Please notify this office in writing within fifteen (15) working days from the date you receive this letter, of the specific steps you have taken to correct the noted violations, including an explanation of how you plan to prevent these violations, or similar violations, from occurring again. Include all documentation of the corrective action you have taken. If you plan to make any corrections in the future, include those plans with your response to this letter as well. If the documentation is not in English, please provide a translation to facilitate our review.

Your response should be sent to the Food and Drug Administration, Center for Devices and Radiological Health, Office of Compliance, Division of Enforcement A, Dental, Ear, Nose, Throat, and Ophthalmic Devices Branch, 2098 Gaither Road, Rockville, Maryland 20850 USA, to the attention of Ronald L. Swann, Branch Chief.

If you need help in understanding the contents of this letter, please contact Ronald L. Swann at the above address or at (240) 276-0115 or FAX (240) 276-0114.

Sincerely yours,

Timothy A. Ulatowski
Director
Office of Compliance
Center for Devices and
Radiological Health